

AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application:

1. - 11. (Canceled)
12. (Withdrawn) A probe whose nucleotide sequence is complimentary to DNA of HPV, which is selected from the group consisting of SEQ ID NOS: 1 to 19 and complementary sequences thereto.
13. (Withdrawn) A Human Papillomavirus (HPV) genotyping kit which comprises:
 - (i) a DNA chip with probes that have nucleotide sequences complementary to DNA of HPV;
 - (ii) primers for amplifying DNA obtained from clinical samples by PCR; and,
 - (iii) means for labeling amplified DNA hybridized with the probes of the said DNA chip.
14. (Withdrawn) The HPV genotyping kit of claim 13 wherein the probe is at least one selected from the group consisting of SEQ ID NOS: 1 to 19 and complementary sequences thereto.
15. (Withdrawn) The HPV genotyping kit of claim 13 or claim 14 wherein the DNA chip further comprises position markers to locate probes.
16. (Withdrawn) The HPV genotyping kit of claim 13 or claim 14 wherein the primers are selected from the group consisting of GP5+ having SEQ ID NO. 22, GP6+ having SEQ ID NO. 23, GP5d+ having SEQ ID NO. 24 and GP6d+ having SEQ ID NO. 25.
17. (Withdrawn) The HPV genotyping kit of claim 13 or claim 14 wherein the means for labeling is a biotin-binding material.
18. (Withdrawn) The HPV genotyping kit of claim 17 wherein the biotin-binding material is streptavidin-R-phycoerythrin.

19. (Withdrawn) A Human Papillomavirus (HPV) genotyping kit which comprises:

(i) a DNA chip with one or more probes selected from the group consisting of SEQ ID NOS: 1 to 19 and complementary sequences thereto, whose nucleotide sequences are complementary to DNA of HPV;

(ii) primers consisting of GP5+ having SEQ ID NO. 22, GP6+ having SEQ ID NO. 23, GP5d+ having SEQ ID NO. 24 and GP6d+ having SEQ ID NO. 25 for amplifying DNA obtained from clinical samples by PCR; and,

(iii) biotin for labeling amplified DNA hybridized with the probes of the said DNA chip and streptavidin-R-phycoerythrin as a biotin-binding material.

20. (Withdrawn) A process for preparing a DNA chip which comprises the steps of:

(i) preparing 5' terminal amine-linked DNA probes which have nucleotide sequences complementary to DNA of HPV;

(ii) affixing the DNA probes thus prepared to an aldehyde-derivatized surface of solid support; and,

(iii) reducing excessive aldehydes not reacted with amine.

21. (Withdrawn) The process for preparing a DNA chip of claim 20 wherein the probe is at least one selected from the group consisting of SEQ ID NOS: 1 to 19 and complementary sequences thereto.

22. (Withdrawn) The process for preparing a DNA chip of claim 9 wherein the concentration of probes which react with aldehyde-derivatized solid surface ranges from 100 to 300pmol/ μ l.

23. (Withdrawn) The process for preparing a DNA chip of claim 20 wherein affixing DNA probes to aldehyde-derivatized solid surface is performed via Schiff's base reaction between amine and aldehyde groups under an environment of 30 to 40°C and 70 to 100% humidity.

24. (Withdrawn) The process for preparing a DNA chip of claim 9 wherein the reduction of aldehyde is performed by the aid of a reducing agent, NaBH₄.

25. (Withdrawn) A method for diagnosis of Human Papillomavirus (HPV) infection comprising:

(a) amplifying DNA obtained from clinical samples with the primers of an HPV genotyping kit to obtain biotin-containing amplified DNA, wherein the HPV genotyping kit comprises:

(i) a DNA chip comprising a combination of at least two different HPV nucleic acid sequence probes selected from the group consisting of:

SEQ ID NO: 1 or the complementary sequence thereof;

SEQ ID NO: 2 or the complementary sequence thereof;

SEQ ID NO: 3 or the complementary sequence thereof;

SEQ ID NO: 4 or the complementary sequence thereof;

SEQ ID NO: 5 or the complementary sequence thereof;

SEQ ID NO: 6 or the complementary sequence thereof;

SEQ ID NO: 7 or the complementary sequence thereof;

SEQ ID NO: 8 or the complementary sequence thereof;

SEQ ID NO: 9 or the complementary sequence thereof;

SEQ ID NO: 10 or the complementary sequence thereof;

SEQ ID NO: 11 or the complementary sequence thereof;

SEQ ID NO: 12 or the complementary sequence thereof;

SEQ ID NO: 13 or the complementary sequence thereof;
SEQ ID NO: 14 or the complementary sequence thereof;
SEQ ID NO: 15 or the complementary sequence thereof;
SEQ ID NO: 16 or the complementary sequence thereof;
SEQ ID NO: 17 or the complementary sequence thereof;
SEQ ID NO: 18 or the complementary sequence thereof; and
SEQ ID NO: 19 or the complementary sequence thereof,

and a glass slide to which the probes are attached;

(ii) biotin-labeled primers for amplifying DNA obtained from clinical samples; and

(iii) means for labeling amplified DNA that hybridizes with the probes of the DNA chip;

(b) applying the amplified DNA to the DNA chip under conditions which allow hybridization of the amplified DNA to the probes;

(c) applying a biotin-binding label to the hybridized DNA on the chip; and

(d) detecting hybridized DNA on the surface of the DNA chip by detecting the a biotin-binding label,

wherein detection of the biotin-binding label indicates the presence of HPV DNA in the sample which corresponds to the HPV probe to which the DNA is hybridized.

26. (Canceled)

27. (Withdrawn) The method for diagnosis of HPV infection of claim 25, wherein amplifying DNA obtained from clinical samples comprises performing PCR using biotin-16-dUTP.

28. (Canceled)

29. (Withdrawn) The method for diagnosis of HPV infection of claim 25, wherein the primers comprise at least one primer selected from the group consisting of GP5+ having SEQ ID NO: 22, GP6+ having SEQ ID NO: 23, GP5d+ having SEQ ID NO: 24 and GP6d+ having SEQ ID NO: 25.

30. (Canceled)

31. (Withdrawn) The method for diagnosis of HPV infection of claim 25, wherein the biotin-binding material is streptavidin-R-phycoerythrin.

32. (Withdrawn) The method for diagnosis of HPV infection of claim 25, wherein the DNA chip is prepared by a process comprising the steps of: (i) preparing 5' terminal amine-linked DNA probes which have nucleotide sequences complementary to DNA of HPV, (ii) affixing the DNA probes thus prepared to an aldehyde-derivatized surface of the glass slide; and (iii) reducing excessive aldehydes not reacted with amine.

33. (Withdrawn) The method for diagnosis of HPV infection of claim 32, wherein the concentration of probes which react with the aldehyde-derivatized surface of the glass slide is between 100 and 300 pmol/ μ l.

34. (Withdrawn) The method for diagnosis of HPV infection of claim 32, wherein affixing the DNA probes to an aldehyde-derivatized surface of the glass slide comprises performing a Schiff's base reaction between the amine and aldehyde groups under an environment of between 30 and 40°C and between 70 and 100% humidity.

35. (Withdrawn) The method for diagnosis of HPV infection of claim 32, wherein reducing excessive aldehydes not reacted with amine is performed by the aid of a reducing agent, NaBH_4 .

36. (Withdrawn) A method for diagnosis of Human Papillomavirus (HPV) infection comprising:

(a) amplifying DNA obtained from clinical samples with the primers of an HPV genotyping kit to obtain amplified DNA containing the first label; wherein the HPV genotyping kit comprises:

(i) a DNA chip comprising a combination of at least two different HPV nucleic acid sequence probes selected from the group consisting of:

SEQ ID NO: 1 or the complementary sequence thereof;

SEQ ID NO: 2 or the complementary sequence thereof;

SEQ ID NO: 3 or the complementary sequence thereof;

SEQ ID NO: 4 or the complementary sequence thereof;

SEQ ID NO: 5 or the complementary sequence thereof;

SEQ ID NO: 6 or the complementary sequence thereof;

SEQ ID NO: 7 or the complementary sequence thereof;

SEQ ID NO: 8 or the complementary sequence thereof;

SEQ ID NO: 9 or the complementary sequence thereof;

SEQ ID NO: 10 or the complementary sequence thereof;

SEQ ID NO: 11 or the complementary sequence thereof;

SEQ ID NO: 12 or the complementary sequence thereof;

SEQ ID NO: 13 or the complementary sequence thereof;

SEQ ID NO: 14 or the complementary sequence thereof;

SEQ ID NO: 15 or the complementary sequence thereof;

SEQ ID NO: 16 or the complementary sequence thereof;

SEQ ID NO: 17 or the complementary sequence thereof;

SEQ ID NO: 18 or the complementary sequence thereof; and

SEQ ID NO: 19 or the complementary sequence thereof;

and a glass slide to which the probes are attached;

(ii) primers containing a first label for amplifying DNA obtained from clinical samples; and

(iii) means for labeling amplified DNA with a second label, wherein the DNA hybridizes with the probes of the DNA chip;

(b) applying the amplified DNA to the DNA chip under conditions which allow hybridization of the amplified DNA to the probes;

(c) applying the second label to the hybridized DNA on the chip, wherein the second label binds to the first label; and

(d) detecting hybridized DNA on the surface of the DNA chip by detecting the second label,

wherein detection of the second label indicates the presence of HPV DNA in the sample which corresponds to the HPV probe to which the DNA is hybridized.

37. (Withdrawn) The method of claim 36, wherein the first label contains biotin and the second label contains streptavidin.

38. (Withdrawn) The method of claim 36, wherein the biotin-containing label is biotin-16-dUTP and the streptavidin containing label is streptavidin-R-phycoerythrin.

39. (Currently amended) A method for diagnosis of the genotype of Human Papillomavirus (HPV) infection comprising:

(a) amplifying DNA obtained from clinical samples to obtain biotin-containing amplified DNA with using the primers of an HPV genotyping kit ~~to obtain biotin-containing amplified DNA, wherein the HPV genotyping kit comprises comprising:~~

(i) a DNA chip comprising a combination of each of the genotype specific HPV nucleic acid sequence probes set forth as:

SEQ ID NO: 1 or the complementary sequence thereof, specific for HPV genotype HPV-16;

SEQ ID NO: 2 or the complementary sequence thereof, specific for HPV genotype HPV-18;

SEQ ID NO: 3 or the complementary sequence thereof, specific for HPV genotype HPV-31;

SEQ ID NO: 4 or the complementary sequence thereof, specific for HPV genotype HPV-33;

SEQ ID NO: 5 or the complementary sequence thereof, specific for HPV genotype HPV-35;

SEQ ID NO: 6 or the complementary sequence thereof, specific for HPV genotype HPV-39;

SEQ ID NO: 7 or the complementary sequence thereof, specific for HPV genotype HPV-45;

SEQ ID NO: 8 or the complementary sequence thereof, specific for HPV genotype HPV-51;

SEQ ID NO: 9 or the complementary sequence thereof, specific for HPV genotype HPV-52;

SEQ ID NO: 10 or the complementary sequence thereof, specific for HPV genotype HPV-56;

SEQ ID NO: 11 or the complementary sequence thereof, specific for HPV genotype HPV-58;

SEQ ID NO: 12 or the complementary sequence thereof, specific for HPV genotype HPV-59;

SEQ ID NO: 13 or the complementary sequence thereof, specific for HPV genotype HPV-66;

SEQ ID NO: 14 or the complementary sequence thereof, specific for HPV genotype HPV-6;

SEQ ID NO: 15 or the complementary sequence thereof, specific for HPV genotype HPV-11;

SEQ ID NO: 16 or the complementary sequence thereof, specific for HPV genotype HPV-34;

SEQ ID NO: 17 or the complementary sequence thereof, specific for HPV genotype HPV-40;

SEQ ID NO: 18 or the complementary sequence thereof, specific for HPV genotype HPV-42; and

SEQ ID NO: 19 or the complementary sequence thereof, specific for HPV genotype HPV-44,

and a glass slide to which the probes are attached;

(ii) biotin-labeled primers for amplifying DNA obtained from clinical samples; and

(iii) means for labeling amplified DNA that hybridizes with the probes of the DNA chip;

(b) applying the amplified DNA to the DNA chip under conditions which allow hybridization of the amplified DNA to the probes;

(c) applying a biotin-binding label to the hybridized DNA on the chip; and

(d) detecting hybridized DNA on the surface of the DNA chip at a position corresponding to the location of a genotype specific HPV probe by detecting the [[a]] biotin-binding label,

wherein detection of the biotin-binding label indicates the presence of HPV DNA in the sample which corresponds to the genotype of the HPV probe to which the DNA is hybridized.

40. (Currently amended) A method for diagnosis of the genotype of Human Papillomavirus (HPV) infection comprising:

(a) amplifying DNA obtained from clinical samples to obtain amplified DNA containing the first label with using the primers of an HPV genotyping kit to obtain amplified DNA containing the first label; wherein the HPV genotyping kit comprises comprising:

(i) a DNA chip comprising a combination of each of the genotype specific HPV nucleic acid sequence probes set forth as:

SEQ ID NO: 1 or the complementary sequence thereof, specific for HPV genotype HPV-16;

SEQ ID NO: 2 or the complementary sequence thereof, specific for HPV genotype HPV-18;

SEQ ID NO: 3 or the complementary sequence thereof, specific for HPV genotype HPV-31;

SEQ ID NO: 4 or the complementary sequence thereof, specific for HPV genotype HPV-33;

SEQ ID NO: 5 or the complementary sequence thereof, specific for HPV genotype HPV-35;

SEQ ID NO: 6 or the complementary sequence thereof, specific for HPV genotype HPV-39;

SEQ ID NO: 7 or the complementary sequence thereof, specific for HPV genotype HPV-45;

SEQ ID NO: 8 or the complementary sequence thereof, specific for HPV genotype HPV-51;

SEQ ID NO: 9 or the complementary sequence thereof, specific for HPV genotype HPV-52;

SEQ ID NO: 10 or the complementary sequence thereof, specific for HPV genotype HPV-56;

SEQ ID NO: 11 or the complementary sequence thereof, specific for HPV genotype HPV-58;

SEQ ID NO: 12 or the complementary sequence thereof, specific for HPV genotype HPV-59;

SEQ ID NO: 13 or the complementary sequence thereof, specific for HPV genotype HPV-66;

SEQ ID NO: 14 or the complementary sequence thereof, specific for HPV genotype HPV-6;

SEQ ID NO: 15 or the complementary sequence thereof, specific for HPV genotype HPV-11;

SEQ ID NO: 16 or the complementary sequence thereof, specific for HPV genotype HPV-34;

SEQ ID NO: 17 or the complementary sequence thereof, specific for HPV genotype HPV-40;

SEQ ID NO: 18 or the complementary sequence thereof, specific for HPV genotype HPV-42; and

SEQ ID NO: 19 or the complementary sequence thereof, specific for HPV genotype HPV-44,

and a glass slide to which the probes are attached;

(ii) primers containing a first label for amplifying DNA obtained from clinical samples; and

(iii) means for labeling amplified DNA with a second label, wherein the DNA hybridizes with the probes of the DNA chip;

(b) applying the amplified DNA to the DNA chip under conditions which allow hybridization of the amplified DNA to the probes;

(c) applying the second label to the hybridized DNA on the chip, wherein the second label binds to the first label; and

(d) detecting hybridized DNA on the surface of the DNA chip at a position corresponding to the location of a genotype specific HPV probe by detecting the second label,

wherein detection of the second label indicates the presence of HPV DNA in the sample which corresponds to the genotype of the HPV probe to which the DNA is hybridized.